Claims

What is claimed is:

1. A method of producing spatially localized injury to vasculature in a live animal, the method comprising:

targeting vasculature in three dimensions for photodisruption; and

focusing ultrashort laser pulses on the targeted vasculature to produce localized photodisruption.

2. The method of claim 1, further comprising observing physiological parameters in the animal.

3. The method of either claim 1 or claim 2, wherein the step of targeting comprises using a microscope objective.

4. The method of claim 3, wherein the microscope objective has a numerical aperture within a range of 0.1 to 1.3.

5. The method of claim 3, wherein the microscope objective is a component of a two-photon laser scanning microscope.

6. The method of claim 5, further comprising observing the target vasculature using the microscope.

7. The method of claim 1, further comprising observing the target vasculature using optical coherence tomography.

8. The method of either claim 6 or claim 7, wherein the step of observing is performed simultaneously with the photodisruption.

9. The method of claim 1, wherein the step of targeting comprises using optical coherence tomography.

10. The method of any one of claims 1 through 9, wherein the laser pulses have an energy adapted to drive a nonlinear interaction within the target vasculature.

11. The method of any one of claims 1 through 10, wherein the laser pulses have pulsewidths in a range from 10 femtoseconds to 100 picoseconds.

12. The method of any one of claims 1 through 11, further comprising preparing the animal to provide optical access to the vasculature via a transparent window formed in the animal.

13. The method of claim 12, wherein the window is adapted to provide access for insertion of electrical probes.

14. The method of any one of claims 1 through 13, further comprising injecting the animal with a substance for labeling the blood stream.

15. The method of claim 14, wherein the substance is a water-soluble fluorescent tracer or fluorescently-labeled erythrocytes.

16. The method of any one of claims 1 through 15 further comprising measuring blood flow in the targeted vasculature.

17. The method of any one of claims 1 through 16, wherein the localized injury comprises vascular damage of a type selected from among thrombosis, hemorrhage and breach of the blood-brain barrier.

18. A method for in vivo modeling of vascular disorder, comprising:
preparing an animal for optical access to vasculature; and
targeting vasculature in three dimensions for photodisruption; and
focusing ultrashort laser pulses on the target vasculature to produce localized photodisruption, wherein the laser pulses have an energy adapted to drive a nonlinear interaction within the target vasculature.

19. The method of claim 18, wherein the step of targeting comprises using a microscope objective.

20. The method of claim 19, wherein the microscope objective has a numerical aperture within a range of 0.1 to 1.3.

21. The method of either claim 19 or claim 20, wherein the microscope objective is a component of a two-photon laser scanning microscope.

22. The method of claim 21, further comprising observing the target vasculature using the microscope.

23. The method of any one of claims 18 through 21, further comprising observing the target vasculature using optical coherence tomography.

24. The method of either claims 22 or claim 23, wherein the step of observing is performed simultaneously with the photodisruption.

25. The method of any one of claims 18 through 24, wherein the step of targeting comprises using optical coherence tomography.

26. The method any one of claims 18 through 25, further comprising observing physiological parameters within the animal using one or a combination of two-photon laser scanning microscopy, magnetic resonance imaging, functional magnetic resonance imaging, multi-spectral intrinsic imaging, positron emission tomography, time resolved light scattering, Doppler flowmetry, and optical coherence tomography.

27. The method of any one of claims 18 through 26, further comprising observing physiological parameters within the animal using post-mortem histology.

28. The method of any one of claims 18 through 27, wherein the laser pulses have pulsewidths in a range from 10 femtoseconds to 100 picoseconds.

29. The method of any one of claims 18 through 28, wherein preparing the animal comprises forming a window for optical access to the target vasculature.

30. The method of any one of claims 18 through 29, wherein preparing the animal comprises injecting the animal with a substance for labeling the blood stream.

31. The method of claim 30, wherein the substance is a water-soluble fluorescent tracer or fluorescently-labeled erythrocytes.

32. The method of any one of claims 18 through 31 further comprising measuring blood flow in the targeted vasculature.

33. The method of any one of claims 18 through 32, wherein the localized photodisruption comprises vascular damage of a type selected from among thrombosis, hemorrhage, and breach of the blood-brain barrier.

34. A method for observing vascular disease or injury in real time, comprising:

preparing an animal for optical access to vasculature; and

targeting vasculature in three dimensions for photodisruption;

focusing ultrashort laser pulses on the target vasculature to produce localized photodisruption, wherein the laser pulses have an energy adapted to drive a nonlinear interaction within the target vasculature; and

observing physiological parameters of the animal before, during and after photodisruption.

35. The method of claim 34, wherein the step of targeting comprises using a microscope objective.

36. The method of claim 35, wherein the microscope objective has a numerical aperture within a range of 0.1 to 1.3.

37. The method of either claim 35 or claim 36, wherein the microscope objective is a component of a two-photon laser scanning microscope.

38. The method of claim 37, further comprising observing the target vasculature using the microscope.

39. The method of any one of claims 35 through 38, further comprising observing the target vasculature using optical coherence tomography.

40. The method of either claim 38 or claim 39, wherein the step of observing is performed simultaneously with photodisruption.

41. The method of claim 35, wherein the step of targeting comprises using optical coherence tomography.

42. The method of any one of claims 35 through 41, wherein observing comprises using one or a combination of two-photon laser scanning microscopy, magnetic resonance imaging, functional magnetic resonance imaging, multi-spectral intrinsic imaging, positron emission tomography, time resolved light scattering, Doppler flowmetry, and optical coherence tomography.

43. The method of any one of claims 35 through 42, wherein observing after photodisruption comprises using post-mortem histology.

44. The method of any one of claims 35 through 43, wherein the laser pulses have pulsewidths in a range from 10 femtoseconds to 100 picoseconds.

45. The method of any one of claims 35 through 44, wherein preparing the animal comprises injecting the animal with a substance for labeling the blood stream.

46. The method of claim 45, wherein the substance is a water-soluble fluorescent tracer or fluorescently-labeled erythrocytes.

47. The method of any one of claims 35 through 46 further comprising measuring blood flow in the targeted vasculature.

48. The method of any one of claims 35 through 47, wherein the localized photodisruption comprises vascular damage of a type selected from among thrombosis, hemorrhage, and breach of the blood-brain barrier.

49. A device for producing spatially-localized injury to vasculature in an animal, comprising:

an animal mount for holding the animal in a fixed position;

an optical source for producing a photodisruption beam, wherein the photodisruption beam comprises a plurality of ultrashort pulses adapted for driving a nonlinear interaction within the target vasculature; and

a microscope objective for focusing the photodisruption beam onto target vasculature in the animal;

wherein the animal has a window formed therein for providing optical access to the target vasculature.

50. The device of claim 49, wherein the optical source comprises an optical oscillator and an optical pump.

51. The device of either claim 49 or 50, wherein the optical source further comprises an optical amplifier.

52. The device of any one of claims 49 through 51, further comprising detectors for detecting light produced in the animal by the ultrashort pulses.

53. The device of any one of claims 49 through 52, wherein an imaging beam is directed through the microscope objective for imaging the animal.

54. The device of any one of claims 49 through 53, wherein the microscope objective is part of a two photon laser scanning microscope.

55. The device of any one of claims 49 through 53, wherein the microscope objective is part of an optical coherence tomography microscope.

56. The device of any one of claims 49 through 55, wherein the animal mount comprises a kinematic mount for the removal and repositioning of the animal.

57. The device of any one of claims 49 through 56, further comprising a measurement device for observing blood flow in the animal.

58. The device of any one of claims 49 through 57, wherein the ultrashort pulses have pulsewidths in a range from 10 femtoseconds to 100 picoseconds.